IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S) :	Mueller-Walz, et al.	CONFIRMATION. NO.:	5874
SERIAL NUMBER :	10/574,334	EXAMINER :	Kennedy, Nicoletta
FILING DATE :	March 7, 2007	ART UNIT :	1611
FOR :	AEROSOL FORMULATIONS COMPRISING FORMOTEROL FUMARATE DIHYDRATE		

Via EFS

DECLARATION UNDER 37 C.F.R. § 1.132

I, Rudi Mueller-Walz, Ph.D., declare:

1. I am currently Head of Early Development at SkyePharma, A.G. In this position I am responsible for development of oral controlled release formulations, inhaled dosage forms and device development. As evidenced by my *curriculum vitae*, which is submitted with this paper, I have over twenty years of experience in the pharmaceutical industry, with emphasis on the development of products for pulmonary application.

2. The results summarized in **Table 1**, which is submitted with this paper, show the chemical characterization of formoterol fumarate following drying at 80°C. Individual vials with approximately 60 milligrams were prepared and dried in an oven at 80°C under vacuum for 3 days. The heat was turned off at least 12 hours before opening the oven. The vials were immediately tightly closed and stored in plastic bottles containing desiccant. The water content was determined based on the Karl-Fischer ("KF") method. The content of the whole vial was emptied in the KF reagent, so that formoterol fumarate was minimally in contact with ambient humidity. The dried formoterol fumarate was exposed to moisture and allowed to reabsorb water for the specified period of time under normal laboratory conditions, *i.e.*, 20-21°C, 40-45% relative humidity. After the specified time, the vial was tightly closed and stored in a second bottle. Water content was monitored by KF measurements for up to 48 hours of storage. These measurements confirmed that the water content of the sample remained constant when stored as described.

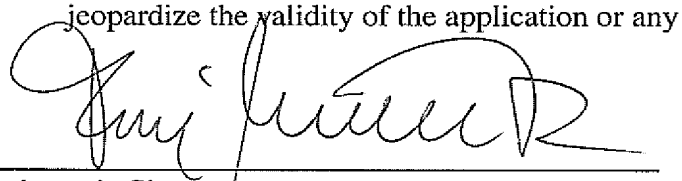
3. The crystalline structure of the formoterol fumarate following its exposure to moisture as described above was analyzed using x-ray powder diffraction (XRPD). The results

demonstrated that this method could distinguish between the anhydrate and dihydrate forms of formoterol fumarate.

4. The results show that a predominantly dihydrate form is produced when the dried formoterol fumarate is exposed to normal laboratory conditions for 15 hours (see Sample 3) such that the water content reaches 4.4%.

5. The results also show that the anhydrate form is present when the water content is slightly lower than 4.4%. Thus, Samples 2 and 4, each containing 3.5% and 4.1% water, respectively, contained the anhydrate form rather than the dihydrate form. It must be noted that XRPD analysis was performed to differentiate between the anhydrate and dihydrate forms and not aimed to quantify the relative amounts of these polymorphs.

6. As a person signing below, I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Title 18, United States Code, § 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.



Declarant's Signature

24 - FEB - 2010

Date

Full Name of Declarant: Rudi Mueller-Walz, Ph.D.

Submitted Herewith:
Curriculum Vitae of Rudi Mueller-Walz, Ph.D.
Table 1

CURRICULUM VITAE

Dr. Rudi Müller-Walz

Home address:
Hans-Vetter-Strasse 108
D-79650 Schopfheim / Germany

Home phone: +49 7622 64 785
Cell phone: +41 178 60 99 533
Work phone: +41 61 467 55 15
e-mail: rudimueller-walz@freenet.de
r.mueller@skyepharma.ch

SUMMARY

A knowledgeable and motivated pharmaceutical expert holding a master degree in chemistry and a doctorate in biophysics, with more than 20 years of experience in pharmaceutical industry, especially in research and development of inhaled drug delivery, together with expertise in pharmaceutical manufacturing, project management and scientific presentation and writing.

EMPLOYMENT HISTORY

Feb 2008 to present: Head of Early Development, SkyePharma AG.
Responsible for SkyePharma's oral controlled release formulations, inhaled dosage forms and device development.

2002 to Feb 2008: Head of Excellence Group Inhalation, SkyePharma AG.
Responsible for technical development of SkyePharma's inhaled drug delivery projects.

1997 to 2001: Head Galenical Development Aerosols&Inhalation, SkyePharma AG.
Responsible for galenical development and the production of inhaled drug products.

1991 to 1996: Head of Galenical Laboratory, Ciba-Geigy AG (now Novartis AG), Basel/Switzerland.
Responsible for technical development of metered dose inhaler formulations.

1988 to 1991: Head of Analytical Laboratory, Ciba-Geigy AG (now Novartis AG), Basel/Switzerland.
Responsible for particle sizing and physical characterization of metered dose inhaler formulations.

ACHIEVEMENTS

Formulation development of at present two approved inhaled drug products and of four actual Phase III clinical products which was successfully achieved within planned timelines.

Good track record of numerous client and internally sponsored technical feasibility studies that were performed and concluded according to plan.

As a production manager manufacture and delivery of a generic metered dose inhaler product for the Swiss market with a good record of quality, supply safety and successfully passed official inspections by the Swiss health authority.

Inventor of several granted patents that provide the basis of SkyePharma's inhalation franchise (including a steady pipeline of applications).

Regular oral and poster presentation at relevant conferences, for example

- Drug Delivery to the Lungs (annual conference organized by Aerosol Society, UK),
- Respiratory Drug Delivery (biannual conference organized by Virginia Commonwealth University, US),
- International Conference for Aerosols in Medicine (biannual conference organized by the International Society for Aerosols in Medicine, ISAM).

Invited contributor to the textbook 'Design of Controlled Release Drug Delivery Systems' (editors: X. Li and B. Jasti), McGraw-Hill 2006.

Company representation at the European Pharmaceutical Aerosol Consortium (EPAG), a multi-company lobby group liaising with the regulatory authorities on development and quality related issues.

Well-established network of contacts within the pharmaceutical industry, with suppliers and academia.

ACADEMIC EDUCATION AND QUALIFICATIONS

Ph.D. 'The binding of Azur B to DNA', Thesis work, University of Freiburg, Germany 1987 ('magna cum laude').

M.Sc. (Chemistry), University of Freiburg, Germany 1982.

Language skills: German (mother language), English (fluent), French (basic)

Computer knowledge: good practice of MS Office package, MS Project and other MS Window-based applications.

PROFESSIONAL AFFILIATIONS

Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik APV, Germany.
Aerosol Society, UK.

PERSONAL DETAILS

Date of birth: 01-July-1955
Nationality: German
Status: married, two daughters (19 and 16 years)
Interests: Arts, jazz music, alpine trekking, climbing and skiing.

Table 1

XRPD sample	Batch no.	Drying	Moisture exposition	Water content†	Chemical Form‡
Sample #1-1	KN 09002	Dried at 80°C	No	0.7%	"anhydrate" (A)
Sample #2-1	KN 09002	Dried at 80°C	110 min.	3.5%	Mix an- and dihydrate
Sample #3-1	KN 09002	Dried at 80°C	15 hrs	4.4%	Dihydrate
Sample #4-1	KN E03013	Dried at 80°C	140 min	4.1%	Mix an- and dihydrate

† Determined by Karl-Fischer titration.
‡ As identified by X-ray powder diffraction analysis (XRPD).